PATENT
Customer No. 22,852
Attorney Docket No. 08702.0071-00000

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

Hyun KIM *et al.*

Application No.: 09/687,281

Filed: October 13, 2000

For: INJECTABLE CARRIER FORMULATIONS OF HYALURONIC ACID DERIVATIVES FOR DELIVERY OF OSTEOGENIC PROTEINS

Group Art Unit: 1651

Examiner: Jon P. Weber

#20
J.P.W.
6/9/03

Commissioner for Patents
Washington, DC 20231

Sir:

DECLARATION UNDER 37 C.F.R. § 1.132

Executed 30 July 03

I, Hyun Kim, do hereby make the following declaration:

1. I am an inventor of the above-captioned application. My curriculum vitae is attached to this declaration as Exhibit 1.

2. I am currently employed as a Staff Scientist in the Pharmaceutical Research & Development, Drug Delivery and Biomaterials Group at Wyeth Research in Cambridge, MA.

3. From 1994 to 1997 I was a graduate student at Brown University under the supervision of Robert Valentini.

4. My field of expertise is the formulation and development of novel drug delivery systems and biomaterial carriers for proteins and drugs. I have specific

expertise in the formulation of injectable and implantable carriers for drugs and in the analysis of drug interactions.

5. I am an inventor of U.S. Patent No. 5,939,974 (Valentini).

6. As an inventor of both the above-captioned application and the cited Valentini patent, I have read and am familiar with both documents.

7. I have read the Office Action dated March 5, 2003, and I understand that Examiner concludes that the disclosure of the Valentini patent renders claims 1-5, 7, and 11 obvious to those skilled in the art as of the filing date of the instant application and that the disclosure of Valentini in combination with U.S. Patent No. 6,187,742 renders claim 6 obvious to those skilled in the art as of the filing date of the instant application.

8. I believe that those skilled in the art would not consider the injectable formulations disclosed and claimed in the pending application to be obvious modifications of the methods and compositions described in Valentini.

9. Valentini describes a solid scaffold carrier for implantation of BMPs. The synthesis of this solid (non-injectable) scaffold includes a step where the hyaluronic acid derivative is in a liquid form. This liquid form is a thick, slurry-like material containing HYAFF® and a pore former (col. 8, line 32).

IMPOSSIBLE to—this to product

10. The liquid intermediate of Valentini is not injectable because it requires a porosity of 60-90% (col. 8, Table I). The amount of pore-former required to achieve this level of porosity is, at minimum, 9-fold greater than the amount of HYAFF® in the composition (col 8, line 32 and Table I). This large amount of pore former poses a significant problem for injectability.

11. The preferred pore former size used by Valentini is 106-600 microns in diameter (col. 8, line 44). Pore formers of this size are too large to be injectable.

12. The pore formers of Valentini are present at inflammatory, non-biocompatible, or superphysiological levels in the liquid intermediate composition. Consequently, these pore formers must be leached out of the scaffold prior to implantation. The leaching process causes the precipitation of the water-insoluble HYAFF® into a partially wet solid state scaffold.

13. In Valentini, BMPs are only added to the final scaffold and not to the liquid intermediate composition.

I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true, and further, that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Dated: 6/2/03 By: _____